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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,922	01/30/2006	Philip John Hogg	05-363	1798

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EXAMINER	
RICCI, CRAIG D	

ART UNIT	PAPER NUMBER
1628	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,922	HOGG, PHILIP JOHN	
	Examiner	Art Unit	
	CRAIG RICCI	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-28* is/are pending in the application.

4a) Of the above claim(s) *6-8 and 24-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-5 and 9-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 May 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/14/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. The amendments filed 12/14/2009 were entered.

Response to Arguments

2. Applicants' arguments, filed 12/14/2009, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

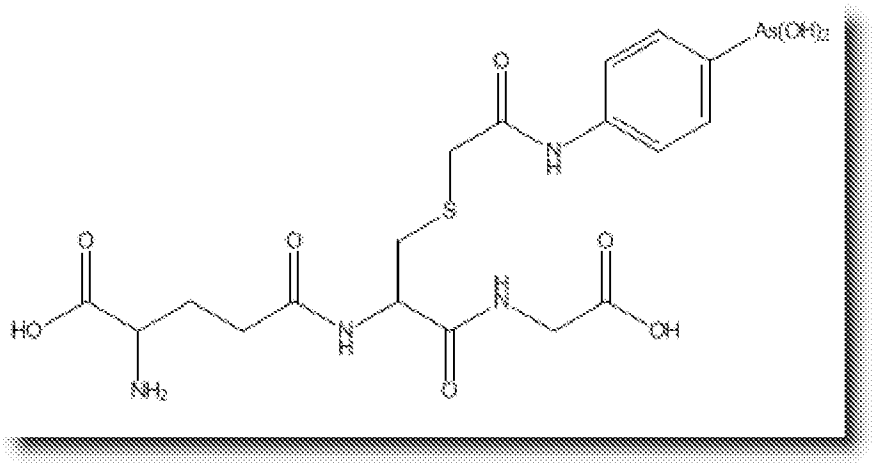
3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. **Claims 1-2 and 4-5 and 9-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Constantini et al* (cited in a previous Action), *Sawada et al* (cited in a previous Action), and *Hogg et al* (cited in a previous Action)**.

5. As amended, instant claims 1-5 are drawn to a process for identifying a compound (or compounds) which selectively induces the mitochondrial permeability transition (MPT) in proliferating cells compared to non-proliferating cells or growth quiescent cells, wherein said method comprises **(A)** contacting a proliferating cell or cell extract with a compound (or compounds) and contacting a non-proliferating cell or growth quiescent cell with said compound (or compounds); **(B)** measuring binding of the compound (or compounds) to the ANT in the

proliferating cell (wherein the compound binds to the ANT in said cell); and **(C)** measuring induction of the MPT in proliferating cells and in non-proliferating or growth quiescent cells (by measuring cytochrome c release and changes in cellular superoxide concentration, as recited by claims 4-5) wherein the compound selectively induces the MPT in the proliferating cells (or cell extract) but not in the non-proliferating or growth quiescent cells (or cell extract). More specifically, as elected by Applicant, the compound to be tested is



. The process, as summarized above, reads on claims 1-2 and 4-5 and 9-23.

6. As previously discussed, and reiterated largely as follows, *Constantini et al* teach that agents which bind ANT induce MPT and cause apoptosis (Abstract; Page 307, Column 2; and Page 311, Column 2). Specifically, *Constantini et al* state that "our data suggest that ANT may be (one of) the critical target molecule(s) responsible for mitochondrial membrane permeabilization and cell death" (Page 311, Column 2). Since "[f]ailure to undergo apoptosis is one of the mechanisms of oncogenesis and/or chemoresistance of transformed cells" (Page 307, Column 1) and since "[m]itochondrial membrane permeabilization is a critical event in the process leading to physiological or chemotherapy-induced apoptosis" (Abstract) the skilled

artisan would have found it *prima facie* obvious that agents which bind ANT, induce MPT, and cause apoptosis could be used as chemotherapeutics in the treatment of cancer, with a reasonable expectation of success. Indeed, *Constantini et al* explicitly motivate the design of such drugs (Page 312, Column 1). However, as noted by *Sawada et al*, "[o]ne of the major problems in human cancer chemotherapy is the nonspecific action of antitumor agents, which can cause unwanted damage to normal [growth quiescent] cells" (Column 1, Lines 19-21). Accordingly, in further view of *Sawada et al*, the skilled artisan would have found it *prima facie* obvious that agents which ***selectively*** bind ANT, induce MPT, and cause apoptosis in proliferating cells (compared to non-proliferating or growth quiescent cells) would be ***especially*** useful chemotherapeutics in the treatment of cancer (compared to agents which are nonselective) since such selective agents would not result in unwanted damage to normal (growth quiescent) cells. Thus, in the treatment of cancer, the skilled clinician would have found it *prima facie* obvious to administer - to a patient in need of cancer treatment - chemotherapeutic agents which **(1)** bind ANT, induce MPT, and cause apoptosis (in view of *Constantini et al*) and **(2)** which do so ***selectively*** in proliferating cells (in view of *Sawada et al*), in order to provide effective chemotherapeutic agents which do not result in unwanted damage to normal (growth quiescent) cells, with a reasonable expectation of success.

7. Chemotherapeutic agents which are useful for the treatment of cancer are well known in the art. In particular, *Hogg et al* teach that the elected compound is useful in the treatment of proliferative diseases, including cancer (compound of formula IV where -As=O is replaced by the arsenoxide equivalent, $-As(OH)_2$; Page 10, Lines 18-19; Page 12, Lines 8-10; Page 13, Lines

29-30; and claims 40-42). However, *Hogg et al* do not specify whether the compound binds ANT, induces MPT, and causes apoptosis ***selectively*** in proliferating cells.

8. Accordingly, it would have been *prima facie* obvious to determine whether the elected compound species (taught by *Hogg et al*) binds ANT, induces MPT, and causes apoptosis ***selectively*** in proliferating cells in order to assess whether the compound would be an especially useful chemotherapeutic in the treatment of cancer, with a reasonable expectation of success. Thus, to evaluate whether the compound species binds ANT, induces MPT, and causes apoptosis ***selectively*** in proliferating cells (compared to non-proliferating cells), it would have been *prima facie* obvious to contact a proliferating cell or cell extract (as well as a non-proliferating cell or growth quiescent cell) with the compound species and monitor each group (i.e., the cancer group (proliferating cell group) and the non-cancer group (non-proliferating cell group)) for ANT binding and MPT (wherein the compound binds ANT and induces MPT in the proliferating cell group, but not the non-proliferating (growth quiescent) cell group). Furthermore, as disclosed by *Constantini et al*, permeabilization of the mitochondria (MPT) is associated with cytochrome c release (Page 301, Column 2). And, as disclosed by *Cai et al*, permeabilization of the mitochondria (MPT) is also associated with an increase in cellular superoxide (Abstract). Accordingly, in measuring compound binding to ANT and induction of MPT, it would have been *prima facie* obvious to measure changes in cytochrome c release and changes in cellular superoxide concentration in the two groups (i.e., the cancer group (proliferating cell group) and the non-cancer group (non-proliferating cell group)) following exposure to the compound species, and to identify a compound that selectively binds ANT and induces MPT in the proliferating cell group but not the non-proliferating cell group.

9. Thus, for all of the foregoing reasons, instant claims 1-2, 4-5 and 9-23 are rejected as *prima facie* obvious.

10. In the previous Action, Applicant argued that "the results of the presently claimed method could not have been predictable nor would one of ordinary skill in the art have a reasonable expectation of success at the time the present invention was made because it was unknown at the time that MPT could be selectively induced in proliferating cells compared to non-proliferating or growth quiescent cells" (Applicant Argument, Page 18). However, these arguments were not considered persuasive because the claims as previously drafted did **not** require that a compound actually induce MPT in proliferating cells and not non-proliferating cells.

11. Applicant now argues that "[t]he claims have been amended herein to recite that the compound selectively induces the MPT in a proliferating cell compared to a non-proliferating cell… Until the applicants discovered that compounds that bind to ANT and selectively induce the MPT in fact existed, there could have been no reasonable expectation that the presently claimed methods, which recite binding of a compound to ANT and selective induction of the MPT, would ever be successful… without any knowledge or expectation of the existence of compounds that bind to ANT and selectively induce MPT, the successful application of the presently claimed methods was not predictable" (Applicant Argument, Pages 19-20).

12. Applicant's arguments are not, however, considered persuasive. The instant claims are drawn to a method of identifying a compound which - ***successfully*** - selectively binds ANT and induces the MPT in a proliferating cell but not in a non-proliferating cell. Notably, the claims are **NOT** drawn to a method of selectively binding ANT and inducing the MPT in a proliferating

cell but not in a non-proliferating cell by administering a compound, even though said selective binding of ANT and induction of the MPT in a proliferating cell but not in a non-proliferating cell is a required outcome of the method as recited. This is a critical distinction since, as discussed above, it would have been desirable at the time the invention was made to identify a compound which selectively binds ANT and induces the MPT in a proliferating cell but not in a non-proliferating cell even if it was unpredictable whether such a compound existed. And, in order to identify such a compound, the skilled artisan would have found it *prima facie* obvious to test compounds (such as the instantly elected compound species) according to the recited method and would have reasonably predicted that, **IF** such a compound exists and is tested, the method as claimed would **predictably** identify said compound by ***successfully*** measuring selective binding of ANT and induction of MPT in the proliferating cell group. On the other hand, if the claims were drawn to a method of selectively binding ANT and inducing the MPT in a proliferating cell but not in a non-proliferating cell by administering a compound (such as the instantly elected species), Applicant's arguments may be persuasive. In that instance, it would appear (based on the prior art applied in the instant Action) persuasive that one of ordinary skill in the art (with no knowledge of compounds that bind to ANT and selectively induce the MPT) would not have predicted the elected compound species to have such activity. But the claims are not so drafted. As discussed above, the claims are drawn to a ***method of identifying a compound*** which does, in fact, bind to ANT and selectively induce the MPT. And the skilled artisan would have reasonably predicted that the claimed method would predictably identify such a compound with a reasonable expectation of success if such compound exists and is treated according to the process.

13. Accordingly, the rejection of claims is maintained.

Conclusion

No new ground(s) of rejection are presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571) 270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Padmanabhan "Paddy" Sreenivasan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/
Examiner, Art Unit 1628

/Brandon J Fetterolf/
Primary Examiner, Art Unit 1642